REMARKS/ARGUMENTS

The foregoing amendments in the specification and claims are of a formal nature, and do not add new matter.

Prior to the present amendment, Claims 28-47 were pending in this application and were rejected on various grounds. Claims 36-37 and 41-43 have been canceled without prejudice. The rejection of the remaining claims is respectfully traversed.

Claims 28-35, 38-40 and 44-47 are pending after entry of the instant amendment.

Applicants expressly reserve the right to pursue any canceled matter in subsequent continuation, divisional or continuation-in-part applications.

Specification

The specification has been amended to remove embedded hyperlink and/or other forms of browser-executable code. Further, Applicants have amended the specification to comply with the provisions of the Budapest Treaty.

Priority

2a. The Examiner had stated that Applicants were entitled to the priority of U.S. Application No. 09/946,374, filed September 4, 2001 based on chondrocyte re-differentiation assay (Example 150, Assay 110).

Applicants respectfully submit that the chondrocyte re-differentiation assay for support of patentable utility was first disclosed in International Application No. PCT/US00/04342, filed on February 18, 2000, the priority of which is claimed in the present application. Accordingly, the present application is entitled to at least the February 18, 2000 priority. In support, page 523 of the PCT publication, WO 00/78961, corresponding to PCT Application No. PCT/US00/04342, is enclosed herewith.

Claim Rejections – 35 U.S.C. §112, First Paragraph

3a. Claims 28-33 are rejected under 35 U.S.C. §112, first paragraph, allegedly "because the specification, while being enabling for an isolated nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO:116, an isolated nucleic acid comprising a nucleotide sequence which completely hybridizes to the nucleotide sequence set for in SEQ ID

NO:115, said nucleic acid encoding the polypeptide of SEQ ID NO:116, does not reasonably provide enablement for an isolated nucleic acid having at least 80%, 85%, 95% or 99% sequence identity to the nucleic acid of SEQ ID NO:115 or to nucleic acid which encodes the polypeptide of SEQ ID NO:116". (See page 3 of the instant Office Action). The Examiner further alleges that "[t]he specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims."

Applicants respectfully disagree and traverse the rejection.

Without acquiescing to the Examiner's position, and solely in the interest of expediting prosecution in this case, Claims 28-32 (and, as a consequence, those claims dependent from the same) have been amended to recite a functional limitation wherein the claimed nucleic acid molecules encode a polypeptide which "induces chondrocyte re-differentiation." Applicants submit that the specification provides ample enablement for such polypeptides based on the *in vitro* data provided in the chondrocyte re-differentiation example (Example 153). Coupled with the general knowledge in the art at the time of the invention, Applicants submit that the present application provides sufficient guidance to one skilled in the art to use the invention without undue experimentation. As the M.P.E.P. states, "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-charge cell Culture Microcarriers, 221 USPQ 1165, 1174* (Int'l Trade Comm'n 1983), *aff'. sub nom., Massachusetts Institute of Technology v A.B. Fortia,* 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985) M.P.E.P. 2164.01.

Further, Applicants respectfully submit that Claim 33 is directed to the nucleic acid sequence of SEQ ID NO: 115 and to the nucleic acid sequence *encoding* the polypeptide of SEQ ID NO: 116. Therefore, the claimed nucleic acid sequences are clearly enabling based on the *in vitro* data provided in the chondrocyte re-differentiation example (Example 153). As the Examiner admitted, the specification is "enabling for ... nucleic acid encoding the polypeptide of SEQ ID NO: 116." (See page 3 of instant Office Action).

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

3b. Claims 28-47 are rejected under 35 U.S.C. §112, first paragraph, for alleged lack of sufficient written description. The Examiner asserts that "[t]he instant claims 28-32 are drawn to an isolated nucleic acid that shares '80%, 85%, 90%, 95% or 99%' identity to the nucleic acid of SEQ ID NO:115, and claims 41-47 are drawn to an isolated nucleic acid which hybridize to a nucleic acid encoding a specific polypeptide. However, the instant specification only describes the structure of the nucleic acid of SEQ ID NO:115, and therefore, conception is not achieved until reduction to practice has occurred. With respect to claims drawn to nucleic acid encoding the 'extracellular domain' of the polypeptide of SEQ ID NO:116, instant specification does not disclose the structure of said extracellular domain." (See page 5 of the instant Office Action).

Applicants submit that the cancellation of Claims 36-37 and 41-43 renders the rejection of these claims moot.

Without acquiescing to the Examiner's position, and solely in the interest of expediting prosecution in this case, Claims 28-32 (and, as a consequence, those claims dependent from the same) are amended to recite a polypeptide that "induces chondrocyte re-differentiation". Furthermore, as amended, Claims 28-33 (and, as a consequence, those claims dependent from the same) no longer recite the term "extracellular domain". Therefore, the recited biological activity, coupled with a well defined, and relatively high degree of sequence identity is believed to sufficiently define the claimed genus, such that one skilled in the art would readily recognize that the Applicants were in the possession of the invention claimed at the effective filing date of this application. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Claim Rejections – 35 U.S.C. §112, Second Paragraph

4. Claims 41-47 are rejected under 35 U.S.C. § 112, second paragraph, allegedly as "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." The Examiner alleges that, the phrase "...Hybridizes under stringent conditions..." is a conditional term and renders the claims indefinite.

Applicants submit that the cancellation of Claims 41-43 renders the rejection of these claims moot.

Accordingly, Applicants respectfully request that the rejection of Claims 44-47 under

35 U.S.C. §112, second paragraph, be withdrawn.

Claim Rejections – 35 U.S.C. §102(b)

5a. Claims 28-33 are rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Baker *et al.*, WO 00/12708 (publication date March 9, 2000).–As discussed above, Applicants are entitled to an effective filing date of February 18, 2000. Accordingly, Baker *et al.* is not prior art under 102(b) since its publication date is after the effective priority date of the present application. Hence, Applicants respectfully request that this rejection be withdrawn.

5b. Claims 41-43 are rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Waterston, R.H. (Accession Number AC019238; published August 17, 2000). Applicants submit that the cancellation of Claims 41-43 renders the rejection of these claims moot.

CONCLUSION

All claims pending in the present application are believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for an extension of time, or credit overpayment to Deposit Account No. **08-1641** (Attorney's Docket No. **39780-2830 P1C46**). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: September 28, 2004

By: _____
Anna L. Barry (Reg. No. 51,436)

HELLER EHRMAN WHITE & McAULIFFE LLP
275 Middlefield Road
Menlo Park, California 94025
Telephone: (650) 324-7184
Facsimile: (650) 324-0638

EXAMPLE 149: Detection of PRO Polypeptides That Affect Glucose or FFA Uptake by Primary Rat Adipocytes (Assay 94)

This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by adipocyte cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by adipocytes would be beneficial including, for example, obesity, diabetes or hyper- or hypo-insulinemia.

In a 96 well format, PRO polypeptides to be assayed are added to primary rat adipocytes, and allowed to incubate overnight. Samples are taken at 4 and 16 hours and assayed for glycerol, glucose and FFA uptake. After the 16 hour incubation, insulin is added to the media and allowed to incubate for 4 hours. At this time, a sample is taken and glycerol, glucose and FFA uptake is measured. Media containing insulin without the PRO polypeptide is used as a positive reference control. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as stimulators of glucose and/or FFA uptake in this assay: PRO1265, PRO1283, PRO1279, PRO1303, PRO1306, PRO1325, PRO1565 and PRO1567.

The following PRO polypeptides tested positive as inhibitors of glucose and/or FFA uptake in this assay: PRO1194, PRO1190, PRO1326, PRO1343, PRO1480, PRO1474, PRO1575 and PRO1760.

EXAMPLE 150: Chondrocyte Re-differentiation Assay (Assay 110)

This assay shows that certain polypeptides of the invention act to induce redifferentiation of chondrocytes, therefore, are expected to be useful for the treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis. The assay is performed as follows. Porcine chondrocytes are isolated by overnight collagenase digestion of articulary cartilage of metacarpophalangeal joints of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm^2 in Ham F-12 containing 10% FBS and 4 μg/ml gentamycin. The culture media is changed every third day and the cells are then seeded in 96 well plates at 5,000 cells/well in 100μl of the same media without serum and 100 μl of the test PRO polypeptide, 5 nM staurosporin (positive control) or medium alone (negative control) is added to give a final volume of 200 μl/well. After 5 days of incubation at 37°C, a picture of each well is taken and the differentiation state of the chondrocytes is determined. A positive result in the assay occurs when the redifferentiation of the chondrocytes is determined to be more similar to the positive control than the negative control.

The following polypeptide tested positive in this assay: PRO1265, PRO1250, PRO1430, PRO1356, PRO1275, PRO1274, PRO1286, PRO1273, PRO1283, PRO1279, PRO1306, PRO1325, PRO1343, PRO1418, PRO1565, PRO1474, PRO1787, PRO1556 and PRO1801.

EXAMPLE 151: Induction of Pancreatic β-Cell Precursor Proliferation (Assay 117)

This assay shows that certain polypeptides of the invention act to induce an increase in the number of pancreatic β-cell precursor cells and, therefore, are useful for treating various insulin deficient states in mammals, including diabetes mellitus. The assay is performed as follows. The assay uses a primary culture of mouse fetal pancreatic cells and the primary readout is an alteration in the expression of markers that represent